

## TEST PLAN FOR m-DIISOPROPENYLBENZENE (CAS NO. 3748-13-8)

### OVERVIEW

Cytec Industries Inc. agrees to sponsor m-diisopropenylbenzene (CAS No. 3748-13-8) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. The company hereby submits a test plan for this substance. It is the intent of the sponsoring company to use existing data discussed in the test plan combined with new studies to fulfill the Screening Information Set (SIDS) endpoints.

## TABLE OF CONTENTS

1.	Introduction.....	3
2.	Designation of Test Substance.....	3
3.	Criteria for Determining Adequacy of Data .....	3
4.	Discussion of Available Test Information .....	5
4.1	Chemical and Physical Properties .....	5
4.1.1	Melting Point .....	5
4.1.2	Boiling Point.....	5
4.1.2	Vapor Pressure.....	5
4.1.4	Octanol/Water Partition Coefficient.....	5
4.1.5	Water Solubility.....	6
4.1.6	Summary/Test Plan for Physical Properties .....	6
4.2	Environmental Fate/Pathways .....	6
4.2.1	Photodegradation .....	7
4.2.2	Stability in Water.....	7
4.2.2	Fugacity .....	7
4.3.4	Biodegradation.....	7
4.3.5	Summary/Test Plan for Environmental Fate Parameters .....	8
4.3	Ecotoxicity.....	8
4.3.1	Acute Toxicity to Fish .....	8
4.3.2	Acute Toxicity to Aquatic Invertebrates .....	9
4.3.3	Acute Toxicity to Aquatic Plants.....	9
4.3.4.	Summary/Test Plan for Ecotoxicity .....	9
4.4	Human Health Data .....	10
4.4.1	Acute Mammalian Toxicity.....	10
4.4.2	Repeated Dose Mammalian Toxicity .....	10
4.4.3	Genetic Toxicity .....	11
4.4.4	Reproductive and Developmental Toxicity .....	11
4.4.5	Additional Data.....	12
4.4.6	Summary/Test plan for mammalian toxicity .....	12
5.	Summary .....	12
6.	References.....	13
7.	Appendix I - Robust summaries.....	15

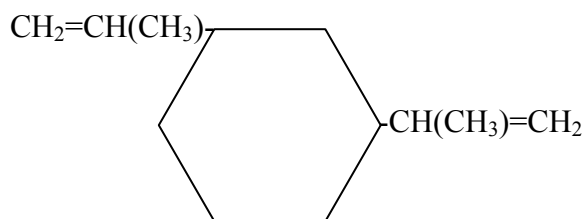
## 1. Introduction

Cytec Industries Inc. submits this test plan for hazard review under the Environmental Protection Agency High Production Volume Chemical Program. The technical contact at this company is:

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## 2. Designation of Test Substance

The test substance presented in this test plan is 1,3-diisopropenylbenzene (CAS No. 3748-13-8). Its chemical structure is as follows:



This substance is known by the following synonyms:

m-diisopropenylbenzene  
meta-diisopropenylbenzene  
benzene, 1,3-bis(1-methylethenyl)-  
m-bis(1-methylvinyl)benzene  
m-DIPEB (Cytec trade name)

The material will be referred to as m-diisopropenylbenzene in the test plan.

M-diisopropenyl benzene is manufactured at one facility in the United States. It is shipped by tank car or tank truck to a Cytec Industries Inc. facility where it is used as an industrial intermediate converted to diisocyanate monomer. About 1% of this substance is drummed and shipped to another facility in the United States for use in optical products. An additional 5 % (approximately) is exported. Manufacture takes place in closed systems, as does conversion to diisocyanate monomer. Based on manufacture at one facility and its predominate use as a closed system industrial intermediate, there is relatively limited opportunity for exposure to this chemical.

## 3. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards

of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate. The m-diisopropenylbenzene test plan matrix (as shown in Table 1) was constructed after a careful evaluation of all existing data (see Sections 4.1- 4.46 below).

Table 1. Test Plan Matrix for m-diisopropenylbenzene

<b><u>CAS No. 3748-13-8</u></b>	Information	OECD Study	Other	Estimation	GLP	Acceptable	New Testing Required
<b>ENDPOINT</b>	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
<b>PHYS/CHEM PROPERTIES</b>							
Melting Point	Y	N	Y	N	N	Y	N
Boiling Point	Y	N	Y	N	N	Y	N
Density	Y	N	Y	N	N	Y	N
Vapor Pressure	Y	N	Y	Y <sup>1</sup> /N <sup>2</sup>	N	Y	N
Partition Coefficient	Y	N	Y	Y	N	Y	N
Water Solubility	Y	N	Y	N	N	Y	N
<b>ENVIRONMENTAL FATE</b>							
Photodegradation	Y	N	Y	Y	N	Y	N
Stability in Water	Y	N	Y	N	N	Y	N
Transport between Environmental Compartments (Fugacity)	Y	N	Y	Y	N	Y	N
Biodegradation	Y	Y	N	N	Y	Y	N
<b>ECOTOXICITY</b>							
Acute Toxicity to Fish	Y	N	Y	N	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	N	Y	N	Y	Y	N
Toxicity to Aquatic Plants	Y	Y	N	N	Y	Y	N
<b>TOXICOLOGICAL DATA</b>							
Acute Toxicity	Y	N	Y	N	Y <sup>3</sup> /N <sup>4</sup>	Y	N
Repeated Dose Toxicity	Y	N	Y	N	Y	Y	N
Genetic Toxicity-Mutation	Y	Y	N	N	Y	Y	N
Genetic Toxicity-Chromosomal Aberrations	N	N	N	N	N	N	Y
Toxicity to Reproduction	N	N	N	N	N	N	Y
Developmental Toxicity	N	N	N	N	N	N	Y
<b>OTHER TOXICITY DATA</b>							
Skin Irritation (NR)	Y	N	Y	N	N	Y	N
Eye Irritation (NR)	Y	N	Y	N	N	Y	N
Sensitization (NR)	Y	N	Y	N	Y	Y	N

Y = yes; N = no

<sup>1</sup> at 25 degrees C; <sup>2</sup> at > = 69.3 degrees C; <sup>3</sup> oral study; <sup>4</sup>inhalation and dermal studies

This matrix is arranged by study type (columns) and screening data endpoints (rows), and indicates if data are provided for each end point in the set of robust summaries.

#### 4. Discussion of Available Test Information

##### 4.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 2.

Table 2. Chemical/physical properties of m-diisopropenylbenzene

Endpoint	Value
Melting point (° C)	-38 to -40 <sup>a</sup>
Boiling point (° C)	231 <sup>a</sup>
Vapor pressure (hPa)	0.1 (at 25° C) <sup>b</sup> 3.1 (at 69.3° C) <sup>a</sup> 990.6 (at 231° C) <sup>a</sup>
Partition coefficient (Log Pow or Kow)	4.89 <sup>b</sup>
Water solubility (mg/l at 25° C)	5.6 <sup>a</sup> 5.0 <sup>b</sup>

<sup>a</sup>measured; <sup>b</sup> estimated by EPIWIN

##### 4.1.1 Melting Point

A measured melting point of -38 to -40°C was recently determined for m-diisopropenylbenzene (Rivera, C. 2002) following ASTM E-794 (standard test method for melting and crystallization temperatures by thermal analysis). The purity of the test substance was 98.9%. The EPIWIN/MPBPWIN model (v.1.40) estimates a value of -14°C.

##### 4.1.2 Boiling Point

A measured boiling point of 231°C is listed on the Material Safety Data Sheet (Cytec Industries Inc., 2002). The purity of the m-diisopropenylbenzene was 100%.

##### 4.1.2 Vapor Pressure

Vapor pressures have been measured for m-diisopropenylbenzene at several temperatures (Cytec Industries Inc., unpublished information). These values include a pressure of 3.1 hPa at 69.3° C and 990.6 hPa at 231° C. EPIWIN/MPBPWIN (v.1.40) estimates a vapor pressure of approximately 0.1 hPa at 25° C, which is generally consistent with the measured value of 3.1 hPa at 69.3°C.

##### 4.1.4 Octanol/Water Partition Coefficient

A log Kow value of ca. 4.89 was estimated by EPIWIN KOWWIN (v1.66), with the

values for the CAS No. and boiling point (231 degrees C) being inputted. The program calculates the log Kow based on molecular structure and an algorithm that sums up individual contributions for the chemical fragments present in the molecule. This positive value is consistent with a non-polar aromatic substance with no water-soluble functional groups, which would be expected to have a high affinity for organic solvents, such as octanol.

#### 4.1.5 Water Solubility

A measured water solubility value of 5.6 mg/l at room temperature has recently been determined for m-diisopropenylbenzene (Stanek, 2002). The purity of the test substance was 98.9%. The EPIWIN/WSKOW program (v.1.40) estimated a water solubility of 5 mg/l based on an inputted log Kow of 4.89.

#### 4.1.6 Summary/Test Plan for Physical Properties

Measured values are available for melting point, boiling point, vapor pressure and water solubility. The log Kow (partition coefficient value) was obtained using EPIWIN and is consistent with the molecular structure of the test substance and with its measured low water solubility value. The available data are sufficient to characterize the physical properties of m-diisopropenylbenzene as an organic liquid with relatively high boiling point, low vapor pressure and low water solubility. No further testing for these endpoints is planned.

### 4.2 Environmental Fate/Pathways

The results of environmental fate modeling and studies are summarized in Table 3 below.

Table 3. Environmental fate parameters for m-diisopropenylbenzene

Endpoint	Value
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant) <sup>a</sup> (Atmospheric T <sub>1/2</sub> ) <sup>a</sup>	ca 1.04 x 10 <sup>-11</sup> cm <sup>3</sup> /(molecule*sec) 1.225 hours
Stability in Water	No reliable measured or estimated data <sup>b</sup>
Henry's Law Constant <sup>a</sup>	3.48 x 10 <sup>-3</sup> atm-m <sup>3</sup> /mol
Koc <sup>a</sup>	4036
Environmental transport (Fugacity Level III mass percentages) <sup>a</sup>	Air = 0.214 Water = 24.9 Soil = 63.9 Sediment = 11.0
Biodegradation <sup>c</sup>	Not readily biodegraded

<sup>a</sup> Estimated using EPIWIN

<sup>b</sup> The test substance does not possess functional groups generally recognized to be readily hydrolyzable in water under neutral ambient conditions.

<sup>c</sup> Measured value

#### 4.2.1 Photodegradation

Photodegradation with hydroxyl radical sensitizer was estimated using EPIWIN/AOP (v1.90). An overall OH rate constant of  $ca\ 1.04 \times 10^{-11}\ \text{cm}^3/(\text{molecule} \cdot \text{sec})$  was calculated based on the summation of individual rate constants for each bond fragment in the molecule using the program algorithm. A half-life of 1.225 hours was calculated assuming a constant concentration of OH radical and pseudo first order kinetics. No information was found with respect to direct photolysis of m-diisopropenyl benzene, but hydroxyl radical-induced photodegradation would be expected to remove the substance from the atmosphere quickly.

#### 4.2.2 Stability in Water

An attempt was made to estimate the rate of hydrolysis for m-diisopropenylbenzene using the EPIWIN/HYDROWIN program (v1.67). This estimation method, however, is valid only for molecules containing certain functional groups, including esters, carbamates, amides, and halomethanes. Measured hydrolysis data are not available. The test substance contains no functional groups generally recognized to readily undergo hydrolysis under neutral ambient conditions. Therefore, hydrolysis of this material is not likely to take place readily, especially at neutral ambient, conditions. Carbon-carbon double (olefinic) bonds are not readily attacked by water, but olefinic bonds can react with cold concentrated sulfuric acid via addition of a proton ( $\text{H}^+$ ) followed by addition of sulfate anion ( $\text{HSO}_3^-$ ) to form the alkyl sulfuric acid, which can then undergo hydrolysis to form the corresponding alcohol (Fieser and Fieser, 1957). However, since this reaction is not likely to occur in natural waters, one may conclude that hydrolysis of m-diisopropenylbenzene is unlikely to be an important degradative process in the environment.

#### 4.2.2 Fugacity

Level III fugacity modeling has been conducted on the test material using the EPIWIN model. Measured inputs to the program are melting point ( $-39^\circ\text{C}$ ), boiling point ( $231^\circ\text{C}$ ), vapor pressure (1 mm Hg), and water solubility (5 mg/l). The value inputted for vapor pressure is the measured value extrapolated down to 25 degrees C. The results indicate that the test substance will partition in increasing preference to air, sediment, water and soil. A calculated Henry's Law Constant (the ratio of volatility to water solubility) of  $3.48 \times 10^{-3}\ \text{atm} \cdot \text{m}^3/\text{mol}$  suggests that the test substance has some limited tendency to volatilize from water to the atmosphere. The value is consistent with the material having low volatility, but also having a limited affinity to water. A water soil partition constant (Koc) of 4036 has been estimated using EPIWIN PCKOC (v1.66). This value indicates that the test substance possesses slight soil mobility.

#### 4.3.4 Biodegradation

An OECD Test Guideline 301D (Close Bottle Test) has been conducted with 2 mg/l of a test material containing 97.5-99.1% m-diisopropenylbenzene (Drozdowski, 1987a). Under the conditions of the study, the test material did not biodegrade. At the

concentration tested, the test material was not soluble. To increase surface area and immersion and reduce partitioning, the test material was applied to a carrier. Because the ability of the carrier to promote degradation of insoluble substances was not demonstrated with a reference material, the study was given a reliability rating of 2 (valid with restrictions).

The results of this study are not inconsistent with what one might expect based on the molecular structure of the test substance. m-Diisopropenylbenzene is an aromatic substance with non-polar olefinic side chains. A substance with this structure has limited solubility in water, and possesses no functional groups that are readily vulnerable to biodegradation.

#### 4.3.5 Summary/Test Plan for Environmental Fate Parameters

The environmental fate parameters discussed above indicate that the test substance, when released to the air, will readily undergo photodegradation (atmospheric half life ca 1.2 hours). However, some atmospheric material may be washed into the hydrosphere. Material released to water has some tendency to volatilize (Henry's Law Constant  $3.48 \times 10^{-3}$  atm-m<sup>3</sup>/mol), but is expected to biodegrade slowly. As a result of limited solubility, material released to water in significant quantity is likely to be deposited in soil or sediment as well as air (due to some volatilization). The material is not likely to be strongly persistent in the environment, because it does have some soil mobility (estimated Koc = 4036) and can volatilize slowly to the atmosphere, where it readily undergoes photodegradation. Sufficient data exist to characterize the environmental fate parameters at the screening level and no testing for these endpoints is planned.

### 4.3 Ecotoxicity

The results of studies and ECOSAR modeling are summarized in Table 4 below.

Table 4. Ecotoxicity of m-diisopropenylbenzene

Endpoint	Value	
	Experimental (mg/l)	ECOSAR (mg/l)
Toxicity to fish (96-hr LC <sub>50</sub> )	6.2	0.225
Toxicity to Daphnia (48-hr LC <sub>50</sub> )	4	0.295
Toxicity to Algae (96-hr EC <sub>50</sub> )	4.92	0.218

#### 4.3.1 Acute Toxicity to Fish

A static GLP study in fathead minnows was performed with a material containing 99.13% m-DIPEB (Bowman, 1986). The no observable effect concentration (NOEC) and lethal concentration in 50% of the organisms (LC<sub>50</sub>) in this 96-hour study were 1.2 and 6.2 mg/l, respectively. None of the fish exposed to  $\leq 2.5$  mg/l and all fish exposed to 20 mg/l died



by 96 hours. This study was given a reliability rating of 2 (valid with restrictions) since concentrations of test material were not analytically confirmed and the results may have been influenced by insolubility of the test material at 10 and 20 mg/l. The 96-hour LC<sub>50</sub> value for fish estimated by the EPA's ECOSAR model (v0.99) is 0.225 mg/l, which is approximately an order of magnitude less than the measured value.

#### **4.3.2 Acute Toxicity to Aquatic Invertebrates**

A static, GLP study in *Daphnia magna* was performed with a test material containing 99.13% m-diisopropenylbenzene (Forbis et al., 1986). The NOEC and LC<sub>50</sub> values in this 48-hour study were 1 and 4 mg/l, respectively. None of the *Daphnia* exposed to ≤ 1.8 mg/l and all organisms exposed to 5.6 and 10 mg/l died by 48 and 24 hours, respectively. An oily film was present on the surface of water containing 5.6 and 10 mg/l, suggesting that the material might not be completely soluble at these concentrations. The study was given a reliability rating of 2 (valid with restrictions) since concentrations of test material were not analytically confirmed. The EPA's ECOSAR model (v0.99) predicts a 48-hour EC<sub>50</sub> value of 0.295 mg/l for *Daphnia*, which is approximately an order of magnitude less than the measured value.

#### **4.3.3 Acute Toxicity to Aquatic Plants**

The toxicity of m-diisopropenylbenzene (98.3% pure) to *Selenastrum capricornutum* was tested according to OECD Test Guideline 201 (Drozdowski, 1987b). For this test, the index of toxicity is inhibition of growth rate. The NOEC, and effective concentration in 50% of the organisms (EC<sub>50</sub>) at 96 hours were 1.77 and 4.92 mg/l, respectively. No growth occurred in cells exposed to 18 mg/l for 96 hours. In this study, there was no mention of the higher concentrations (10 and 18 mg/l) being insoluble. Based on results of the other aquatic toxicity tests, it is likely that the material was not completely soluble at these concentrations. Since concentrations of test material were not analytically confirmed, the study was given a reliability rating of 2 (valid with restrictions). The 96-hour EC<sub>50</sub> value calculated for green algae by the ECOSAR model (v0.99) is 0.218 mg/l, which is approximately an order of magnitude less than the measured value.

#### **4.3.4 Summary/Test Plan for Ecotoxicity**

Results of adequate studies in fathead minnows, *Daphnia magna* and *Selenastrum capricornutum* show that m-diisopropenylbenzene is of moderate toxicity to these species. For all the species tested, the average no effect concentrations and EC/LC<sub>50</sub> values were approximately 1 and 5 mg/l. In all the studies, the LC<sub>50</sub> values are likely to have been influenced by slight insolubility at the highest concentrations used (10 to 20 mg/l). As shown by Rivera (2002), the solubility limit of the material is 14 mg/l. Since the higher concentrations used in the aquatic toxicity studies did not appear to be completely soluble, the amount of test material available to the organisms at these concentrations was probably less than the nominal concentrations. Therefore, the actual EC/LC<sub>50</sub> values are likely to be slightly lower than those determined in the experimental studies.

Results of ECOSAR modeling suggest that the EC/LC<sub>50</sub> values for fish, *Daphnia* and

algae are approximately an order of magnitude less than measured values. These values are considered to be conservative estimates of the toxicity of the material to aquatic organisms. No additional testing is necessary.

## **4.4 Human Health Data**

### **4.4.1 Acute Mammalian Toxicity**

This endpoint is filled by two sufficient oral toxicity studies in rats (Calkins, 1981a; Chow, 1981a), two inhalation studies in rats (Myers, 1986; Nachreiner, 1986), and one dermal toxicity study in rabbits (Chow, 1981b). The oral and dermal LD<sub>50</sub> values (lethal doses in 50% of the animals) were 13.2 ml/kg (approximately 12,200 mg/kg) and > 2000 mg/kg (the highest concentration tested), respectively. The LC<sub>50</sub> value for aerosol inhalation was between 0.545 mg/l (the LC<sub>0</sub>) and 5.576 mg/l (the LC<sub>100</sub>). The purity of the test material used in all the acute studies was at least 97.5%. The oral study conducted by Calkins and the inhalation study conducted by Nachreiner are considered to be the critical studies for the endpoint, and were given reliability ratings of 1 (valid without restriction).

Clinical signs observed in rats treated orally with 5.0 to 20 ml/kg m-diisopropenylbenzene included diarrhea, lacrimation, lethargy, urine-soaked fur, nasal discharge, alopecia, crusty nose and eyes, and cold body temperature (Calkins, 1981a; Chow, 1981a). Four out of five males treated with 20 ml/kg exhibited alopecia/edema around the anus. Most of the signs were present only for the first days of the study (with the exception of alopecia, which generally appeared a week after treatment). The frequency or variety of signs did not appear to increase with increasing doses of test material, and did not exhibit any sex-related trends (with the exception of alopecia/edema around the anus of high dose males). The only effect noted in rabbits treated dermally with 2000 mg/kg m-diisopropenylbenzene after abrading the skin was slight dermal irritation (Chow, 1981b).

In rats exposed to 5.576 mg/l (5,576 mg/m<sup>3</sup>) m-diisopropenylbenzene aerosol for 6 hours by inhalation, signs of toxicity such as wet fur, red perinasal wetness, lacrimation, whole body tremors, dermal irritation, hyperactivity, ataxia, and mouth breathing were observed during the first 90 minutes of exposure (Nachreiner, 1986). A complete loss of motor activity was observed in these animals for the remainder of the exposure period. After exposure, all animals exhibited absent toe, tail pinch, and surface righting reflexes, hypothermia, respiratory difficulties, wet fur, and dermal irritation. All of the animals appeared to be moribund before death (which occurred within 24 hours of exposure). In rats inhaling the nonlethal concentration (0.545 mg/l or 545 mg/m<sup>3</sup>), ocular irritation occurred during exposure. By contrast, no signs of toxicity were observed in rats exposed to a saturated atmosphere of m-diisopropenylbenzene vapor for 6 hours (Myers, 1986).

### **4.4.2 Repeated Dose Mammalian Toxicity**

A 28-day inhalation toxicity test (5 days per week for 4 weeks) with 107, 510, and 970 mg/m<sup>3</sup> m-diisopropenylbenzene (98.3% pure) has been performed in rats. Rats were

predominantly exposed to vapor at 107 mg/m<sup>3</sup> and approximately 50% vapor at 970 mg/m<sup>3</sup>. The estimated percentage of respirable particles at 510 and 970 mg/m<sup>3</sup> was 86% and 89%, respectively. Exposure to 970 mg/m<sup>3</sup> m-diisopropenylbenzene was associated with decreased weight and weight gain in males, increased numbers of segmented neutrophils in the blood of both males in females, increased urine volume in males, increased liver weight, and increased concentrations of serum enzymes that are markers for liver toxicity. Effects observed at 510 mg/m<sup>3</sup> included reduced weight gain in males early on in the study, and increased urine volume and relative liver weight in males (without any changes in clinical chemistry parameters or pathology). Symptoms of eye irritation were observed in 1/10 animals exposed to 107 mg/m<sup>3</sup> and 6/10 animals exposed to 510 or 970 mg/m<sup>3</sup>. Since study personnel did not consider the effects observed at 510 mg/m<sup>3</sup> to be indicative of systemic toxicity, they assigned a no observable adverse effect level (NOAEL) of 510 mg/m<sup>3</sup>. However, since the effects observed at this concentration were also observed at 970 mg/m<sup>3</sup>, they appear to be related to treatment. Since no systemic effects were observed at 107 mg/m<sup>3</sup>, this concentration appears to be a more accurate estimation of the NOAEL.

#### **4.4.3 Genetic Toxicity**

##### **4.4.3.1 Mutagenicity**

m-Diisopropenylbenzene (98.36% pure) has been tested for mutagenicity in an OECD Test Guideline 471 study conducted with *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and *E. coli* strain WP2uvra- (Thompson and Bowles, 1999). In these tests, the highest concentrations of m-diisopropenylbenzene that did not cause excessive toxicity were not mutagenic in the absence or presence of a metabolic activation system.

##### **4.4.3.2 Chromosomal Aberration**

No tests for this endpoint were located. Testing is proposed for this endpoint (using OECD Test Guideline 473).

#### **4.4.4 Reproductive and Developmental Toxicity**

No reproductive or developmental toxicity tests with m-diisopropenylbenzene have been performed. Results of the 28-day study indicate that inhalation of up to 970 mg/m<sup>3</sup> has no effect on the histopathology of the ovaries and testes. This suggests that the material has no effect on reproduction. However, since this study was conducted for 28, rather than 90 days, it cannot be used to fill the reproductive toxicity endpoint.

According to established guidelines of the HPV chemical program, chemicals that are used solely as intermediates are exempt from reproductive toxicity testing. Since there is minor use of the test substance (about 1% of total use) that may disqualify the material as being used solely as a closed system intermediate (see Section 2), an oral OECD Test Guideline 421 Study (Reproduction/Developmental Screening Test) will be conducted.

#### **4.4.5 Additional Data**

##### **4.4.5.1 Skin and Eye Irritation**

Adequate studies in rabbits show that 100% pure m-diisopropenylbenzene is slightly irritating to skin and moderately irritating to eyes (Chow, 1981b,c). Effects observed in the robustly conducted eye irritation study consisted of conjunctival redness, chemosis and/or discharge. Nasal discharge was observed in 3/9 animals a few days after exposure. No irritation to the cornea or iris was observed.

##### **4.4.5.2 Sensitization**

Results of a well-conducted GLP study in guinea pigs indicate that 100% pure m-diisopropenylbenzene is a sensitizer (Calkins, 1981b). Animals receiving induction applications of undiluted test material exhibited a dose-dependent dermal contact sensitization response when challenged with 100% test material and rechallenged with 12.5, 25, 50 and 100% test material.

#### **4.4.6 Summary/Test plan for Mammalian Toxicity**

Adequate studies with m-diisopropenylbenzene have been conducted for all endpoints except chromosomal aberration and reproductive/developmental toxicity. Acute oral, inhalation and dermal studies show that acute exposure to fairly large amounts of m-diisopropenylbenzene is required to cause lethality. Signs of nervous system toxicity are observed prior to death in rats exposed to 5,576 mg/m<sup>3</sup> m-diisopropenylbenzene by inhalation. Symptoms of toxicity observed in animals exposed to nonlethal concentrations of m-diisopropenylbenzene (by any route) are consistent with its ability to cause irritation to the skin and eyes. A well-conducted study in guinea pigs shows that m-diisopropenylbenzene is sensitizing. Results of the 28-day repeated dose inhalation study in rats show that exposure to 510 mg/m<sup>3</sup> m-diisopropenylbenzene produces adaptive changes in the liver (i.e. increased liver weight), and exposure to 970 mg/m<sup>3</sup> causes increased release of enzymes from the liver (but no pathologic changes). Adequate studies show that m-diisopropenylbenzene is not mutagenic or clastogenic.

Testing for chromosomal toxicity and reproductive/developmental toxicity will be conducted since data do not exist for these endpoints. The tests that will be performed will conform to OECD Test Guidelines 473 and 421, respectively.

### **5. Summary**

In summary, valid data are present to satisfy all physical/chemistry, and environmental endpoints (with the exception of chromosomal aberrations and reproductive/developmental toxicity). Testing for chromosomal aberrations and reproductive/developmental toxicity is planned. Existing studies on acute, repeated dose, and genetic toxicity (mutations) are sufficient to satisfy these endpoints. Data for eye and skin irritation and sensitization are adequate (although not required).

## 6. References

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